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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,482	01/02/2002	Irun R. Cohen	COHEN=42A	5950

28765 7590 05/24/2004

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EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 05/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,482	COHEN ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/445,602.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/2/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group XXXII, claims 8-11 drawn to a peptide of SEQ ID NO:21, in Paper of 3/25/04 is acknowledged. It is noted that SEQ ID NO:11 is contained in SEQ ID NO:21 and as such will be examined with SEQ ID NO:21 and the restriction between Groups XXXII and XXII is vacated and GROUPS XXXII and XXII will be examined together. The traversal is on the ground(s) that the inventions are not independent and a proper search of the peptide claims would obtain art on the use of the peptides and this application is based on a PCT and unity of invention is fulfiled and a search of any peptide can be easily compared to the 17 specific peptides and are readily searchable through the PTO database (see pages 2-3 of response). This is not persuasive. Although the peptides are in the same class and subclass each peptide has a distinct structure and a search would have to be performed on each one. While the peptides are searchable on the PTO database, each peptide is distinct and art on one would not be art on the others. In addition, as stated in the restriction requirement, the peptides are distinct from the methods of use. Also the arguments about this application being based on a PCT and unity of invention should be fullfiled is not persuasive because this application was filed under 111 not 371. As to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each

group. For these reasons the restriction requirement is deemed to be proper and is made **FINAL**.

2. Claims 1-7, 8-11 in part are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions. Applicant timely traversed the restriction (election) requirement in Paper of 3/25/04.

3. Claims 8-11 are under examination being examined to the extent the peptide is either SEQ ID NO:11 or SEQ ID NO:21.

Specification

4. The disclosure is objected to because of the following informalities:

a. The first line of the specification needs to be updated to add that application 09/445,602 is abandoned.

Appropriate correction is required.

Claim Objections

5. Claims 8-11 are objected to because of the following informalities: The claims encompass non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 8-11 are indefinite for reciting "and salts and chemical derivatives thereof" because the exact meaning of the phrase is not clear. Does the phrase mean a composition comprising the peptide or a compound claim wherein the peptide is a derivative or salt form?

b. Claims 8-11 are indefinite for reciting "eliciting antibodies to p53" because the peptide contains a sequence from a CDR of an anti-p53 Mab and it is unclear if the peptides elicit an AB3 response or an AB1 response.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a peptide of a CDR containing SEQ ID NO:11 or SEQ ID NO:21. The specification teaches that SEQ ID NO:11 is CDR3 of the light chain of the 240 mAb and SEQ ID NO:21 is from the VL of the 240 mAb which is SEQ ID NO:11 and residues on either side of the CDR3. The claims encompass a multitude of peptides that contain SEQ ID NO:11 and are capable of eliciting an immune response to p33 but also contain additional residues on both side of the peptide which is not described except for SEQ ID NO:21 (and SEQ ID NO:21 can also have additional residues because of the open language of the claims). Thus, the structure of the peptide sequences are not defined. With the exception of SEQ ID NO:11 and 21 the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Thus, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed.

10. Claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide consisting of the VL of the 421 antibody of Jannot et al (see below)(containing SEQ ID NO:11), does not reasonably provide enablement for a peptide capable of eliciting antibodies to p53 wherein the peptide contains just any sequence of a CDR from just any anti-p53 antibody and salts and chemical derivatives thereof. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to any peptide which contains a CDR sequence from an anti-p53 antibody and is capable of eliciting an immune response to p53 and peptides containing SEQ ID NO:11 or 21 and salts and chemical derivatives thereof wherein the response is an anti-p53 response.

The specification teaches production of anti-p53 antibodies with immunization of SEQ ID NO:21 (see page 37). The specification does not teach production of anti-p53 antibodies it teaches production of anti-idiotype antibodies for an anti-tumor response (see Example 4) . The specification does not teach production of an anti-id response with just any CDR peptide or any chemical derivative thereof. The specification teaches that chemical derivative is a peptide that contains additional chemical moieties not "normally part of the peptide" (see page 20).

The claims are not commensurate in scope with the enablement provided in the specification. As taught by Erez-Alon et al (Cancer Res. 58:5447-5452, 1998) not all

peptides from a CDR of an anti-p53 antibody are capable of eliciting an immune response against p53 (see page 5449 and the Pab-248 mab and peptides from CDRs thereof). In addition, Law et al (EP 0438312A2, 1/17/91) teach the exact sequence of SEQ ID NO:21 and 11 (see Figure 3A) and the sequence is from CDR3 of an anti-CD18 antibody. Thus, because of the polymorphic nature of the immunoglobulin genes and sequences there are antibodies that have CDR sequences that are in anti-p53 antibodies that do not bind p53 in other antibodies. Thus, the art demonstrates that not all CDRs from an anti-p53 antibody can elicit anti-p53 antibodies and in addition, the CDR sequences are not specific for anti-p53 antibodies. In addition, antibodies are directed to specific sequences as antigens and one skill in the art would not conclude that one could chemically derivatize a peptide that is from a CDR of a anti-p53 antibody and still produce antibodies to p53. In fact even those peptides that are from a CDR of an anti-p53 antibody did not elicit antibodies as evidenced from Erez-Alon et al.

In addition, it is known in the art that antibodies directed to antibodies produce anti-idiotypic antibodies which mimic the antigen and are not antibodies that bind the antigen as encompassed by the claims.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Jannot et al (BBRC 230:242-246, 1/1997).

The claims recite a synthetic peptide capable of eliciting antibodies to p53 which contain a CDR sequence of SEQ ID NO:11 of an anti-p53 antibody. For this rejection because of the indefinite nature of the claims the claims are interpreted as a peptide which is capable of eliciting anti-idiotypic antibodies to p53.

Jannot et al teach the 421 scFv peptide of the VL which has the CDR sequences of SEQ ID NO:11 and the antibody is from an anti-p53 mAb (see Figure 4). Since the specification does not disclose the length of a peptide the VL reads on the claims.

Althought the claims require a synthetic peptide these are a product by process claims, thus, the method in which the peptides were produced is immaterial to their patentability. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

In addition since the peptide is from an anti-p53 Mab it would inherently produce anti-idiotypic antibodies.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571) 272-0871.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832

LARRY R. HELMS, PH.D
PRIMARY EXAMINER